Amendments to the Claims

This listing of claims will replace all prior versions and listings of the claims in the application.

Listing of claims

Claim 1 (previously presented) An effervescent pharmaceutical formulation for the sustained and controlled oral administration of a pharmaceutically effective amount of a drug selected from a calcium channel blocker, an ACE inhibitor, a narcotic analgesic or analogues or combinations thereof, said formulation comprising microcapsules having a D50% between about 100 nm and 900 nm in which the drug is entrapped in a biodegradable polymer and in which the pH of the formulation is adjusted to optimize delivery of the drug, wherein the formulation is adapted to disperse upon addition of water to form an effervescent drink.

Claim 2 (cancelled)

Claim 3 (previously presented) An effervescent pharmaceutical formulation according to Claim 1, wherein the formulation is used to deliver the drug to a patient on a once-daily basis so as to achieve a therapeutic effect over a substantially 24 hour period.

Claim 4 (cancelled)

Claim 5 (previously presented) An effervescent pharmaceutical formulation according to claim, wherein the drug loading of the microcapsules ranges from about 10% to 70% by weight.

Claim 6 (currently amended) An effervescent pharmaceutical formulation for the sustained and controlled oral administration of a pharmaceutically effective amount of a drug selected from a calcium channel blocker, an ACE inhibitor, a narcotic analgesic or a combination thereof, the formulation comprising drug-loaded biodegradable microcapsules having a D 50% between about 100 nm and 900 nm and a drug loading which ranges from about 10% to 70% by weight and wherein the pH of the formulation is adjusted to optimize delivery of ~~the~~ each drug.

Claim 7 (previously presented) An effervescent pharmaceutical formulation according to Claim 6, which can be used to deliver the drug to a patient on a once-daily basis so as to achieve a therapeutic effect over a substantially 24 hour period.

Claim 8 (previously presented) An effervescent pharmaceutical formulation according to claim 1, wherein the microcapsules have a D 50% between about 200 nm and 400 nm.

Claim 9 (previously presented) An effervescent pharmaceutical formulation according to claim 1, wherein the drug loading of the microcapsules ranges from about 20% to 50% by weight.

Claim 10 (previously presented) An effervescent pharmaceutical formulation according to claim 1, wherein the drug is selected from diltiazem, verapamil, nifedipine, nimodipine, nicardipine, hydromorphone, codeine sulfate, oxycodone, dihydrocodeine tartrate, oxycodeinone, morphine, fentanyl, sufentanil, oxymorphone, buprenorphine, captopril, enalapril, lisonopril and mixtures thereof.

Claim 11 (previously presented) An effervescent pharmaceutical formulation according to Claim 10, wherein the drug is a mixture of nifedipine and hydromorphone.

Claim 12 (previously presented) A pharmaceutical formulation of Claim 1, wherein the microcapsules comprise a polymer matrix, said polymer matrix comprising a polymer selected from the group consisting of polylactide, polyglycolide, poly(lactic acid-co-clycolic acid, poly(e-caprolactone), poly(hydroxybutyric acid); polyorthoesters; polyacetals, polydihydropyrans, polycyanoacrylates, polypeptides, cross-linked polypeptides, and stereoisomers, racemic mixtures, co-polymers and polymer mixtures thereof.

Claim 13 (previously presented) A pharmaceutical formulation according to Claim 12, wherein the polymer matrix comprises poly-D,L-lactide.

Claim 14 (currently amended) A pharmaceutical formulation according to claim 1, wherein the release profile measured in accordance with the Paddle Method of U.S. Pharmacopoeia XX at ~~37∞C~~ 37°C and 75 rpm for ~~the or~~ each drug is substantially as follows:

a) 10-30% release within 2 hours after administration;
b) 30-60% release within 4 hours after administration;
c) 60-80% release within 8 hours after administration; and
d) $\geq$80% release within 24 hours after administration.

Claim 15 (currently amended) A pharmaceutical formulation according to Claim 1, wherein the release profile measured in accordance with the Paddle Method of U.S. Pharmacopoeia XX at ~~37∞C~~ 37°C and 75 rpm for ~~the or~~ each drug is substantially as follow:

a) 10-40% release within 1 hour after administration;
b) 20-60% release within 4 hours after administration;

c) 40-80% release within 8 hours after administration; and

d) $\geq$80% release within 16 hours after administration.

Claim 16 (previously presented) A method for the manufacture of microcapsules according to Claim 1, which comprises the steps of:

a) dissolving or dispersing a drug and a biodegradable polymer in a solvent to form a mixture;

b) microfluidising said mixture into an external phase to form an emulsion in which the emulsion droplets have a mean diameter less than 1 mm; and

c) stirring said emulsion to form microcapsules having a size (D 50%) between about 100 nm and 900 nm.

Claim 17 (cancelled)

Claim 18 (cancelled)

Claim 19 (cancelled)

Claim 20 (cancelled)

Claim 21 (previously presented) The effervescent pharmaceutical formulation of Claim 1, wherein the drug is diltiazem or a combination of diltiazem and an narcotic analgesic or an ACE inhibitor and wherein the pH of the formulation is greater than 7.

Claim 22 (previously presented) The effervescent pharmaceutical formulation of Claim 1, wherein the drug is hydromorphone or a combination of hydromorphone and a

calcium channel blocker or an ACE inhibitor and wherein the pH of the formulation is less than pH 6 or greater than pH 7.

Claim 23 (new) The formulation of claim 1 wherein said microcapsules are prepared from an emulsion comprising a suspension medium and suspended therein droplets having a mean droplet diameter of less than 1 micron, said droplets comprising the drug and said encapsulating polymer.

Claim 24 (new) The formulation of claim 23 wherein said biodegradable polymer is selected from polylactide, polyglycolide, poly(lactic acid-co-clycolic acid, poly(∈-caprolactone), poly(hydroxybutyricacid); polyorthoesters; polyacetals, polydihydropyrans, poly cyanoacrylates, polypeptides, cross-linked polypeptides, and stereoisomers, racemic mixtures, co-polymers and polymer mixtures thereof.

Claim 25 (new) The formulation of claim 24 wherein said drug is selected from the group consisting of diltiazem, verapamil, nifedipine, nimodipine, nicardipine, hydromorphone, codeine sulfate, oxycodone, dihydrocodeine tartrate, oxycodeinone, morphine, fentanyl, sufentanil, oxymorphone, buprenorphine, captopril, enalapril, lisonopril and mixtures thereof.

Claim 26 (new) The formulation of claim 25 wherein said biodegradable polymer is poly D,L lactide.

Claim 27 (new) The formulation of claim 26 wherein said drug is a mixture of a calcium antagonist and a narcotic analgesic.

Claim 28 (new) The formulation of claim 27 wherein said calcium antagonist is diltiazem.

Claim 29 (new) The formulation of claim 27 wherein said calcium antagonist is nifedipine.